IN THE CLAIMS:

MARKED-UP COPY OF CORRECTED CLAIMS

1. Reaction chambers coated with native, synthetically or enzymatically prepared nucleic acids, [**characterized in that** the coating ensues with calibrated standard nucleic acids with addition of carrier nucleic acids in a non-covalent manner at chemically or biochemically non-modified surfaces of the inner walls of reaction chambers.] wherein said coating is performed non-covalently with a mixture of calibrated nucleic acids said standard nucleic acids and carrier nucleic acids at the surface of the inner walls of reaction chambers which neither requires chemical nor biochemical modification prior coating."

2. Reaction chambers according to [claim1, **characterized in that]** claim 1, wherein they are comprised of glass or plastic vessels or of glass capillaries.

3. Reaction chambers according to claim 1, [**characterized in that]** wherein said DNA, RNA, synthetic equivalents of DNA and/or RNA, as well as dU-containing DNA are used as standard nucleic acids.

4. Reaction chambers according to claim 1, [**characterized in that]** wherein said, a) for the dilution of DNA standards, a DNA solution is used comprising a minimum sequence homology to the nucleic acid compound to be analyzed, and b) a tRNA solution is used for the dilution of the RNA standards.

5. Reaction chambers according to claim 1, [**characterized in that**, as the carrier nucleic acid, DNA of lamda phages is used, which previously is transferred into easily desorbable fragments] wherein said carrier nucleic acid is DNA of the lambda phage which is converted into readily soluble fragments of a mean length of about 1 - 2 kb by means of ultrasonic treatment.

6. Method for the production of reaction chambers according to claim 1, **[characterized in that]** wherein said calibrated standard nucleic acids and added carrier nucleic acids are directly aliquoted into reaction chambers [suitable for enzymatic amplification], and are subsequently non-covalently adsorbed directly in the inner wall of the reaction chamber by means of freeze-drying or vacuum-centrifugating lyophilization.

7. Method according to claim 6, **[characterized in that]** wherein plastic vessels or glass capillaries are coated.

8. Method according to claim 6, **[characterized in that]** wherein said DNA, RNA, synthetic equivalents and/or RNA, as well as dU-containing DNA are used as nucleic acids.

9. Method according to claim 6, **[characterized in that]** wherein said,

a) for the dilution of DNA standards, a DNA solution is used comprising a minimum sequence homology to the nucleic acid

compound to be analyzed, and b) a tRNA solution is used for the dilution of the RNA standards.

10. Method according to claim 6, **[characterized in that**, as the carrier nucleic acid, DNA of lambda phages is used, which previously is transferred into easily desorbable fragments] wherein said carrier nucleic acid is DNA of a lambda phage which is converted into readily soluble fragments of a mean length of about 1 - 2 kb by means of ultrasonic treatment.

11. Method according to claim 6, [**characterized in that** corresponding reaction chambers are simultaneously coated with a plurality (at least two) of different analyte sequence-specific calibrated nucleic acids, if necessary, or a different cellular or organic origin or originating from different species.] wherein reaction chambers are, if necessary, simultaneously coated with a multitude (i.e. at least two) of application-specific calibrated nucleic acids of different cellular or organic origin, or originating from different species.

12. Method according to claim 6, [**characterized in that** the coating of at least 96 reaction chambers arranged in a microtiter format ensues with at least 12 x 8 sequence-specific standard nucleic acids of decreasing concentrations covering the entire expected concentration range of the analyte nucleic acid to be measured (highest concentration: A1 -12, lowest concentration: H1 - 12).] wherein said coating is performed of at least 96 reaction chambers which are arranged in a microtiter format and which comprise at least 12x 8-well strips containing carrier nucleic acids and calibrated nucleic acids while the arbitrarily choosen concentration of each calibrated nucleic acid differs stepwise from well to well (highest concentration in A1-A12, lowest concentration in H1-H12) in order to cover the entire concentration range of the analyte nucleic acid to be measured.

13. Method according to claim 6, [**characterized in that** the coated reactions chambers are closed standing upright] wherein the coated reaction chambers are sealed and standing upright in an appropriate carrier box receiving at least 96 vessels.

14. Method according to claim 6, [wherein, apart from the calibrated nucleic acids, at least two specific marked or unmarked oligonucleotides acting as primers or probes, the carrier nucleic acid and further reaction components required for the enzymatic amplification are contained in the reaction chambers in a lyophilized form, or specifically marked or unmarked oligonucleotides acting as primers or probes, the carrier nucleic acid and further reaction components required for the enzymatic amplification are contained in separate vessels without nucleic acid standard in a lyophilized form.] wherein apart from the calibrated standard nucleic acids, at least two oligonucleotides acting as primers or probes which are either 5`- and/or 3`- labeled with a fluorescent or non-fluorescent chromophore or unlabeled, the carrier nucleic acid and further components required for enzymatic nucleic acids amplification are contained in the

reaction chambers in a lyophilized formulation, or at least two oligonucleotides acting as primers or probes, the carrier nucleic acid and further components required for enzymatic nucleic acids amplification are contained in separate vessels without said standard nucleic acids in a lyophilized formulation.

15. Method according to claim 6 further comprising

[Use of] using the reaction chambers coated with nucleic acids [according to claim 1] in test kits for the detection of selected nucleic acids in biological substances.

16. Method according to claim 15 further comprising

using [Use according to claim 15, **characterized in that** said] test kits [are] comprised of [at least one ZeptoStrip (] an octet strip of closed reaction chambers coated with eight different nucleic acid concentrations [)] and closed with a film / foil, of at least two oligonucleotides, as well as one carrier nucleic acid.

17. (new) A method for producing reaction chambers comprising employing a chamber wherein calibrated standard nucleic acids and added carrier nucleic acids are directly aliquoted into the chamber, lyophilizing the calibrated standard nucleic acids and the added carrier nucleic acids by freeze-drying or vacuum-centrifugating; and non-covalently adsorbing directly the calibrated standard nucleic acids and the added carrier nucleic acids in the inner wall of the chamber and thereby producing a reaction chamber.

18. (new) The method according to claim 17 further comprising coating plastic vessels or glass capillaries.

19. (new) The method according to claim 17 further comprising employing DNA, RNA, synthetic equivalents and/or RNA, as well as dU-containing DNA as nucleic acids.

20. (new) The method according to claim 17 further comprising employing a DNA solution comprising a minimum sequence homology to the nucleic acid compound to be analyzed for a dilution of DNA standards, and

employing a tRNA solution for a dilution of RNA standards.

21. (new) The method according to claim 17 further comprising employing a DNA of a lambda phage as a carrier nucleic acid, and converting the DNA of the lambda phage into readily soluble fragments of a mean length of about 1 - 2 kb by means of ultrasonic treatment.

22. (new) The method according to claim 17 further comprising simultaneously coating the reaction chamber with a multitude of application-specific calibrated nucleic acids of different cellular or organic origin, or originating from different species.

23. (new) The method according to claim 17 further comprising

performing coating of at least 96 reaction chambers which are arranged in a microtiter format and which comprise at least 12x 8-well strips containing carrier nucleic acids and calibrated nucleic acids while the arbitrarily choosen concentration of each calibrated nucleic acid differs stepwise from well to well (highest concentration in A1-A12, lowest concentration in H1-H12) in order to cover the entire concentration range of the analyte nucleic acid to be measured.

24. (new) The method according to claim 17 further comprising

sealing coated reaction chambers; and

standing the coated reaction chambers upright in an appropriate carrier box receiving at least 96 vessels.

25. (new) The method according to claim 17 further comprising

employing at least two oligonucleotides acting as primers or probes which are either 5`- and/or 3`- labeled with a fluorescent or non-fluorescent chromophore or unlabeled apart from the calibrated standard nucleic acids; containing the carrier nucleic acid and further components required for enzymatic nucleic acids amplification in the reaction chambers in a lyophilized formulation, or at least two oligonucleotides acting as primers or probes; and

containing the carrier nucleic acid and further components required for enzymatic nucleic acids amplification in separate vessels without said standard nucleic acids in a lyophilized formulation.

26. (new) The method according to claim 17 further comprising forming a test kit for a detection of selected nucleic acids in biological substances with the reaction chamber.

27. (new) The method according to claim 17 further comprising forming a test kit comprising an octet strip of closed reaction chambers coated with eight different nucleic acid concentrations and closed with a

film / foil, of at least two oligonucleotides, as well as one carrier nucleic acid.

28. (new) The method according to claim 17 further comprising forming a test kit comprising a strip of eight reaction vesselsl coated with eight different amounts of at least one calibrated standard nucleic acid, carrier nucleic acid and at least two oligonucleotides and which is sealed with an appropriate self-adhesive foil.

29. (new) A reaction chamber obtained by employing a method for producing reaction chambers comprising

employing a chamber wherein calibrated standard nucleic acids and added carrier nucleic acids are directly aliquoted into the chamber;

lyophilizing the calibrated standard nucleic acids and the added carrier nucleic acids by freeze-drying or vacuum-centrifugating; and

non-covalently adsorbing directly the calibrated standard nucleic acids and the added carrier nucleic acids in the inner wall of the chamber and thereby producing a reaction chamber.

REMARKS

Claims 1 through 16 continue to be in the case.

New claims 17 through 28 are being introduced.

The new claims have the following basis:

CLAIM	BASIS
17	claim 6
18	claim 7
19	claim 8
20	claim 9
21	claim 10
22	claim 11
23	claim 12
24	claim 13
25	claim 14
26	claim 15
27	claim 16
28	claim 16

29 claim 6

The Office Action refers to the Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Applicant is submitting an abstract of the Disclosure on a separate sheet.

2. The following guidelines illustrate the preferred layout and content for patent applications.

These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.

(b) (c) (d) (e)

(g) (h) (i) G) (k) (l)

Cross-References to Related Applications.

Statement Regarding Federally Sponsored Research or Development.

Reference to a "Microfiche Appendix" (see 3 7 CFR 1.96).

Background of the Invention.

1. Field of the Invention.

2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.

Brief Summary of the Invention.

Brief Description of the Several Views of the Drawing(s).

Detailed Description of the Invention.

Claim or Claims (commencing on a separate sheet).

Abstract of the Disclosure (commencing on a separate sheet).

Drawings.

Sequence Listing (see 37 CFR 1.821-1.825).

Applicant is amending the specification to include the headings as proposed in the Office Action.

The Specification does not contain the "Brief Description of Drawings" heading for the description of drawings on pages 8 and 9. The only sections of the specification are "Description", "Exemplary embodiments" and "Legends to the Figures".

The present amendment furnishes a "Brief Description of Drawings".

3. The disclosure is objected to because of the following informalities: A sentence on page 3, lines 9-14 is unclear.

Appropriate correction is required.

Applicant is correcting the last paragraph on page 2 to obviate the rejection.

Claim Rejections-35 USC § 112

The following is a quotation of the second paragraph of 3 5 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim

the subject matter which applicant regards as the invention. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

A) Claims 1-16 contain a phrase "...characterized in that...". It is unclear what is its meaning and how it defines the scope of the claims.

The present amendment removes the objectionable language.

B) Claims 1-5 are indefinite because of the following limitations "...the coating ensues with calibrated standard nucleic acids with addition of carrier nucleic acids in a non-covalent manner at chemically or biochemically non-modified surfaces of the inner walls of reaction chambers.".

Applicant is amending the language objected to.

C) Claim 5 is indefinite because of the limitation "...as the carrier nucleic acid, DNA of lambda phagesis used, which

previously is transferred into easily desorbable fragments...".

Applicant is rewording claim 5 to overcome the rejection.

D) Claims 6-14 are indefinite because of the preamble "Method for the reaction chambers...". It is unclear what the method is for.

Applicant is amending the claims to provide corrected language.

E) Claims 6-14 are indefinite because of the limitation "...suitable for enzymatic amplification...". It is unclear what features are defined by this limitation.

Applicant is canceling the language found to be objectionable.

F) Claims 6-14 are indefinite because there are no active method steps in theses claims.

Claims 6 through 14 have been amended to avoid the rejection. In addition, new claims 17 through 35 are being submitted which are also intended to overcome the rejection.

G) Claim 10 is indefinite because of the limitation "...as the carrier nucleic acid, DNA of lambda phagesis used, which previously is transferred into easily desorbable fragments.

Claim 10 is amended to overcome the rejection.

H) ...". H) Claim 11 is indefinite because of the limitation "...reaction chambers are ... coated with a plurality ... of different analyte sequence-specific calibrated nucleic acids, if necessary, or a different cellular or organic origin or originating from different species." It is unclear what the different nucleic acids are.

Claim 11 is amended to avoid the objectionable language.

I) Claim 12 is indefinite because of the limitation "...the coating ... ensues with at least 12x 8 sequence-specific standard nucleic acids...". It is unclear what "coating ensues" means in terms of the method and what is the sequence for which the standard nucleic acids are specific for.

The present amendment changes the language of claim 12.

J) Claim 13 is indefinite because of the limitation "... coated reaction chambers are closed standing upright...". It is unclear what property of the chambers is conveyed by this limitation.

The property "sealed" has now been added to the claim language.

K) Claim 14 is indefinite because of the limitation "...at least two specific marked or unmarked oligonucleotides acting as primers or probes...". It is unclear what these oligonucleotides are specific for and "marked" means for oligonucleotide.

Claim 14 has been amended extensively to overcome the rejection.

L) Claims 15 and 16 provide for the use of reaction chambers, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Claims 15 and 16 are rejected under 35 U.S.C.101 because the claimed recitation of a use, without setting forth any

steps involved in the process, results in an improper definition of a process, i.e.,results in a claim which is not a proper process claim under 3 5 U.S.C. 101. See for example Ex pane Dunki,153 USPQ 678(Bd.App.1967)and Clinical Products, Ltd. v.Brenner,

255 IT Supp.131,149 USPQ 475(D.D.C.1966)

Claims 15 and 16 have been extensively amended and are now presented in method form. It is deemed that the changes will avoid the rejections expressed in the Office Action.

The Office Action refers to Claim Rejections-35 USC § 102.

7. The following rejection is based on the product claimed in claim 1, which is "Reaction chambers coated with native, synthetically or enzymatically prepared nucleic acids", irrespective of

the way in which they were obtained(see MPEP 2113).

8. Claims 1-5 and 15 stand rejected under 3 5 U.S.C. 102(b) as being anticipated by Day et al.

(Biotechniques,vol.18,pp.981-984,1995).

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Day et al. teach 96-well plates coated with DNA templates which were dried in the wells. The plates can then be used for setting up PCR reactions. Alternatively, PCR primers are distributed into the wells and dried there. In both cases, adherence of the dried DNA to the walls of the wells is non-covalent, since both dried template and dried primers function in subsequent PCR reactions (page 381-383).

The reference Day et al. refers to "dried template DNA"and "dried PCR oligonucleotides", but no reference is made to "standard DNA" within the four corners of the Day et al. reference. A reference to "standard nucleic acids" is not necessary in the day et al. reference considering the goals expressed in the Day et al. reference, since the Day et al. reference is concerned with qualitative diagnostics. The molecule precise storage of nucleic acids is of subordinate importance to the Day et al. reference, since all reaction agents are employed in a stochiometric excess. Therefore, the

reference Day et al. in contrast to the present application does not furnish any experimental proof for the proven storage stability and possible concentration losses between the starting state (that is prior to drying) and final product (that is after drying) are not verified.

The present invention in contrast has a different base. The present invention is concerned with a quantitative diagnostic and not with aa qualitative determination. For this reason it is necessarily required according to the present invention to obtain a molecule precise stability and storability of adsorbed standard DNA/RNA in the reaction chamber, since the effective number of molecules present in the starting composition is substantially influencing the course of a reference curve essential for quantification of analytical nucleic acids, wherein the reference curveis generated with the aid of the adsorbed standard DNA/RNA. Therefore, not only the adsorption technology but also the completely quantitative desorption of the standard nucleic acid represent extremely critical parameters, which are both completely resolved together with the aid of the present invention. The reference Day et al. in contrast teaches only an

undefined adsorption of nucleic acids without suggestion to the associated desorption behavior.

The coating of reaction chambers with undefined and unmodified template-DNA as taught in the Day et al. reference is not subject matter of the present invention. In contrast it is a base of the invention method to adsorb exclusively in vitro synthesized, by cloning or fully synthetically produced standard nucleic acid of a defined sequence and concentration with mono-specificity for an analyte, wherein a defined combination of several of such nucleic acid standards represent a further advaage relating to use, wherein several analytes are simultaneously or separately measurable with corresponding sets of Zepto strips (strips consisting of eight reaction vessels) by way of quantitative polymerase chan reaction (PCR), as required in particular in claim 11.

The undefined drying conditions employed by the reference Day et al. (drying over several hours at ambient temperature, Page 892) .in addition would result in a partial lysis with large certainly in particular of the extremely low concentrated standard DNA/RNA molecules. Only very gentle drying in a vacuum-centrifuge or by way of freeze-drying under

precisely defined conditions (that is freezing at –80 degrees centigrade, quick transfer into Lyovac, one hour drying without intermediate thawing) assure a uniformly reproduceable product stability.

Claim 1 of the present apllication is not anticipated by Day et al. reference, since the reference Day et al. does not teach any standard nucleic acids. A further distinction of the present invention relative to the Day et al. reference comprises that carrier nucleic acids are added to the standard nucleic acids. The carrier nucleic acids do effect not only an improved adsorption during the lyophilization process and an increased stability of the standard nucleic acids in the reaction chamber, but serve in addition for the production of a thinning sequence derived from the calibrated standard. A calibration curve as is common in analysis can thereby be produced.

9. No references were found teaching or suggesting claims 6-14, but they are rejected for other reasons.

Applicant very much appreciates that no state of the srt was found relative to claims 6 through 14. It is deemed that the present amendments

will remove the other rejections to claims 6 through 14. Also, claims 17 through 25 recite more clearly the method steps of these claims.

Applicant submits that the prior art made of record neither anticipates nor renders obvious the present invention.
Reconsideration of all outstanding rejections is respectfully requested.

If the Examiner should not be able to find a certain element of Applicant's claims in a search of the state of the art and such element is deemed by the Examiner to be necessary for forming a basis for a rejection, then the Examiner is invited to inform the Applicant of such element in order to allow the Applicant to fully meet their disclosure requirement in view of innumerable and hypothetical possibilities of combining references to allege obviousness of individual claims. In particular, in view of different levels of familiarity of inventors with the information disclosure requirements of the United States Patent and Trademark Office developed in recent years and apparently still developing, which disclosure requirements are believed to be unique in the world, any help and

suggestions regarding possible problems seen by the Examiner are welcome.

All claims as presently submitted are deemed to be in form for allowance and an early notice of allowance is earnestly solicited.

Respectfully submitted,

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